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Assessment of Immune Function Development in Mice Irradiated *in Utero* with 2450-MHz Microwaves

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ABSTRACT

Groups of time-bred pregnant mice were irradiated with 2450-MHz microwaves at an incident power density of 28 mW/cm^2 for 100 min daily from day 6 to day 18 of pregnancy. The average specific absorption rate (SAR) was 16.5 W/kg. Two experiments were performed under these conditions. At 3 and 6 weeks of age the mice were assessed for development of the primary immune response to sheep erythrocytes, *in vitro* mitogen-stimulated lymphocyte proliferation, and natural killer (NK) cell activity. No consistent significant difference in the primary immune response, in the mitogen response, or in the NK cell activity was observed between irradiated and sham-irradiated mice.

INTRODUCTION

In general, more dramatic effects are produced in mammals when they are exposed to a physical or chemical agent during development compared with exposure during adulthood [Wilson, 1973]. By the same token, various toxic agents have their most profound effects on the immune system when the animal is treated with the agent during the development of the immune system [Vos, 1977]. In support of this we reported that *in utero* and early postnatal exposure of rats to 2450-MHz or 425-MHz microwave radiation affects the *in vitro* mitogen-stimulated proliferation of lymphocytes [Smialowicz et al., 1979a, 1981b]. Both T- (thymus-derived) and B- (bursa-equivalent) lymphocytes from 425- or 2450-MHz microwave irradiated rats were found to undergo increased proliferation in the presence of mitogens compared with sham-irradiated controls. These changes in lymphocyte activity occurred when the animals were exposed to microwave radiation at dose rates in excess of their basal metabolic rate (BMR). In contrast, when rats were irradiated *in utero* and during early postnatal life with 100 MHz at an absorbed dose rate of less than their BMR, no effect on lymphocyte activity was observed [Smialowicz et al., 1981a].

Recently, Berman et al. [1978, 1981] reported that pregnant mice irradiated with 2450-MHz microwave radiation at absorption rates in excess of the BMR, bore offspring which showed significant stunting of growth at day 18 of gestation and at 7 days after birth. The present work was performed to determine if such growth retardation is of any functional significance for the developing immune system and also as an extension of our previous work in rats.

MATERIALS AND METHODS

Animals

Time-bred CD-1 mice (Charles River Labs., Willmington, ME) were received in our vivarium two days after breeding (day 1 of breeding is the day a copulatory plug was first seen). Mice were caged singly and allowed food and water *ad libitum*. Animals were maintained on a 12:12 light–dark cycle.

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Microwave Exposure System

Irradiation was conducted in a 2450-MHz exposure facility in which temperature, humidity, and air flow were controlled [Elder and Ali, 1975]. The microwave field was generated by a Varian Model PPS-2.5 AS industrial heating unit at a frequency of 2450 MHz in a continuous-wave mode. A total root-mean-square (rms) ripple of 11% was measured after the installation of a full-wave bridge in the filament circuit. A controlled-environment exposure chamber (61 × 76 × 76 cm) constructed of foamed polystyrene was positioned beneath a 10-dB gain pyramidal-horn antenna in the far field.

The environmental chamber was confined in an electrically anechoic chamber that was lined with microwave-absorbing material (Model CBV24 and VCVB24, Emerson and Cuming, Inc., Canton, MA). The environmental-control system permitted regulation of the temperature and humidity in the exposure chamber and in an identical foamed-polystyrene sham-irradiation chamber located outside of the anechoic chamber. The air temperature was maintained at 22 ± 0.5°C for the first experiment (temperature used in our earlier work [Smialowicz et al., 1979a, 1981a, 1981b]) and 20.2 ± 0.5°C for the second (temperature used by Berman et al. [1978, 1980]), relative humidity at 50 ± 5% and the average lineal air velocity passing through the chambers was 0.31 ± 0.08 m/s for all microwave and sham-irradiation exposures.

Animal Exposures

Bred mice were confined individually in vented-polycarbonate cages, 6 cm square, which were placed in one of 25 positions as described by Berman et al. [1978]. The volume of the polycarbonate cage allowed the mouse freedom of movement during exposure. An equal number of mice were positioned in a similar array in the sham-irradiation chamber. Mice were irradiated for 100 minutes at a power density of 28 mW/cm^2, which results in a SAR (as determined by twin-well calorimetry) of approximately 16.5 W/kg [Berman et al., 1978]. Following exposure, mice were immediately returned to their home cages. Bred mice were so treated on day 6 through day 18 of pregnancy. On the morning after birth live and dead neonates were counted and weighed and the mean live litter weight determined. On the sixth day of age the living offspring were again counted and weighed by litter. Data were analyzed by analysis of variance technique in the computer programs of the Statistical Analysis System [Helwig and Council, 1979]. At 6 days of age, litters were normalized to 4 male pups per litter.

Immunological Assays

At three and six weeks of age two pups from each litter were used to assess immune development using the following assays:

Mitogen Response Assay. Mice were killed by cervical dislocation and spleens were immediately removed under aseptic conditions. Spleen-cell suspensions were prepared in RPMI-1640 medium with 25 mM HEPES (Grand Island Biological Co., Grand Island, NY) containing 100 units/ml penicillin, 100 μg/ml streptomycin and 10% heat-inactivated fetal calf serum. Triplicate microcultures of spleen cells to which were added different mitogens (phytohemagglutinin, concanavalin A, pokeweed mitogen, or *E. coli* lipopolysaccharide) were prepared and the amount of ^{3}H-thymidine incorporated into DNA was determined after 72 hours of culture [Smialowicz et al., 1979b]. Data collected as counts per minute (CPM) were $\log_{10}$ transformed and were analyzed using Student's t-test.

Table 1 Number of live neonates and 6-day body weights of mice born to CD-1 dams irradiated with 2450-MHz microwaves during gestation

Variables	Experiment No. 1		Experiment No. 2	
	Sham	Irradiated	Sham	Irradiated
Bred females	25	25	25	25
No. litters	11	7	9	10
Day 6: live[a]	8.9 ± 2.51	8.3 ± 2.50	10.1 ± 2.80	10.4 ± 2.50
Day 6: weight (g)[a]	3.9 ± 0.43	4.0 ± 0.52	3.1 ± 0.56	2.9 ± 0.44[b]

[a]Values are mean ± SD for litters.
[b]$P < 0.01$, analysis of variance.

Primary Immune Response to Sheep Erythrocytes. Spleen cells from mice were assayed for the presence of IgM antibody-forming cells by a modification of the direct plaque-forming-cell (PFC) assay described by Jerne and Nordin [1963]. Mice were immunized with an intraperitoneal injection of 5×10^8 sheep erythrocytes (SRBC). Four days after immunization the spleens were removed and cells producing IgM anti-SRBC antibody were assayed using SRBC as indicator cells. Serum hemolysin and hemagglutination titers were also determined [Smialowicz, 1979b]. Data were analyzed using Student's t-test.

Natural Killer Cell Assay. Spleen cells, prepared as above for the mitogen assay, were assayed for natural killer (NK) cell activity using the method described by Kiessling et al. [1977]. For target cells the *in vitro* subline YAC-1 (obtained from Dr. Ann Berger, Duke University, Durham, NC) of the Moloney-induced lymphoma YAC of mouse strain A was used. The YAC-1 cells were grown in stationary suspension cultures in RPMI-1640 medium supplemented with 10% heat-inactivated fetal calf serum and antibiotics (100 units/ml of penicillin and 100 μg/ml streptomycin). The cells were washed once and resuspended to 3×10^6 cells/ml in medium and labeled with ^{51}Cr (200 μCi ^{51}Cr as sodium chromate, specific activity 200–500 Ci/g, New England Nuclear) for 1 hour at 37°C. After labeling, the YAC-1 cells were washed 3 times and resuspended to 2×10^5 cells/ml in supplemented RPMI medium.

Labeled YAC-1 cells (2×10^4 in a volume of 100 μl) were added to graded numbers of splenic effector cells (100 μl) in round-bottom microtiter plates (Titertek/Linbro, Flow Labs, Rockville, MD). Three replicates of each effector: target ($E:T$) cell ratio (25:1, 50:1, and 100:1) were incubated for 4 hours at 37°C in an atmosphere of 5% CO_2 and 95% air. At the end of the incubation, the plates were centrifuged for 5 min at 1000 RPM and the supernatant was removed using the Titertek supernatant collection system (Flow Lab). Radioactivity in the supernatant was measured in a gamma counter (Packard Instrument Co.). Spontaneous release of radioactivity was determined by incubating 2×10^4 ^{51}Cr-YAC-1 cells with 200 μl of supplemented RPMI medium. Maximum release was determined by adding Triton X-100 (0.25% V/v) to wells containing 2×10^4 ^{51}Cr-YAC-1 cells. Percentage specific ^{51}Cr release was calculated according to the formula:

$$\frac{E - S}{T - S} \times 100$$

where E is the ^{51}Cr released from the target cells in the presence of spleen cell, S is the spontaneous release of ^{51}Cr, and T is the maximum release of ^{51}Cr upon addition of Triton X-100.

Data collected as percent ^{51}Cr release were arcsine transformed and analyzed using Student's t-test.

RESULTS AND DISCUSSION

The number of litters, the mean live pups per litter and the mean live litter weights on the sixth day of age for the two experiments are shown in Table 1. The data for the mean live litter size and mean litter weights are from litters born only on the 20th day of gestation. Litters of other gestational durations were excluded to prevent confounding of weight values by gestation duration. In the first experiment, no significant difference was observed in the mean live litter weights for pups 6 days old. In fact, the mean litter weight was greater in the irradiated group. In the second experiment, however, a significant decrease in the weight of 6-day-old pups from irradiated dams was observed, which is similar to that reported by Berman et al. [1981]. The inconsistent weight results in this study are

Table 2 Primary antibody response of 6-week-old mice born to dams irradiated with 2450 MHz

Experiment No.	Mean PFC/10^6 Spleen Cells ± SE		Mean PFC × 10^{-5}/Spleen ± SE	
	Sham	Irradiated	Sham	Irradiated
1	2039 ± 385(6)	1925 ± 285(6)	4.47 ± 0.96	3.41 ± 0.63
2	2567 ± 294(8)	3436 ± 279(8)*	3.94 ± 0.31	4.06 ± 0.31

Numbers in parentheses are number of mice tested.
*$P < 0.05$, Student's t-test.

difficult to explain. We irradiated the mice under conditions which were almost identical with those employed by Berman et al. [1981] (the only difference was the ambient temperature, i.e., 20.2°C for Berman versus 22°C in the first experiment and 20.2°C in the second). It is interesting to point out that we observed stunting, as did Berman, when the dams were maintained at 20.2°C (second experiment) but not at 22°C. Our failure to observe a consistent growth retardation may be due to the fact that microwave-induced stunting is so subtle. For example, Berman et al. observed only a 10% reduction in fetal (day 18 of gestation) or neonatal (day 7 but not day 1 after birth) body weight following *in utero* irradiation. We observed no weight reduction in rat pups irradiated perinatally with 100-, 425-, or 2450-MHz [Smialowicz et al., 1979a, 1981a, 1981b], albeit at much lower power densities.

Table 2 shows the primary antibody response to sheep red blood cells for mice 6 weeks old. No difference was observed in the plaque forming cells (PFC) per 10^6 spleen cells or PFC/spleen between sham and irradiated mice in the first experiment. Also, there was no difference in either the hemagglutination or hemolysin titers to SRBC between sham and irradiated mice in this experiment. In the second experiment, a significant ($P < 0.05$) increase in the number of PFC/10^6 spleen cells was observed for irradiated compared with sham-irradiated mice. However, when the total number of PFC per spleen was calculated, no difference was observed between the two groups. Furthermore, no difference was observed in the hemolysin and hemagglutination titers of irradiated compared with sham-irradiated mice in this experiment.

Table 3 shows the *in vitro* mitogen-stimulated response of lymphocytes. Several different concentrations of each mitogen were used; however, only optimal stimulating concentrations of each mitogen are shown. A significant decrease was observed in the amount of ^{3}H-thymidine incorporated by unstimulated (no mitogen) lymphocytes from 6-week-old mice in the first experiment. This decrease was not observed in the second experiment and may in fact be due to a spuriously high ^{3}H-thymidine uptake by the unstimulated cells from the sham-irradiated mice in the first experiment. No other significant differences in mitogen responsiveness were observed. These results are in contrast to earlier work in which we observed an increase in the blastogenic response of lymphocytes from rats irradiated *in utero* during early postnatal life with 2450- or 425-MHz [Smialowicz et al., 1979, 1981b]. Exposure to microwaves during the postnatal period was not done in the present study. It is known that the mouse is not fully mature immunologically until about 8 weeks of age. Irradiation of the mice during the postnatal period may be required for induction of changes in lymphocyte responsiveness, although it was found that *in utero* exposure of rats at 425 MHz caused enhanced lymphocyte responsiveness [Smialowicz et al., 1981b].

Table 3 Mitogen-stimulated response of splenic lymphocytes from 3- and 6-week-old mice born to dams irradiated with 2450 MHz

Age (weeks)	Mitogen (μg/culture)	Mean ^{3}H-TdR Uptake × 10^{-3} ± SE Exp. No. 1 Sham(7)	Exp. No. 1 Irradiated(7)	Exp. No. 2 Sham(11)	Exp. No. 2 Irradiated(11)
3	0	1.8 ± 0.3	1.2 ± 0.2	Not Done	
	PHA − 0.125	37.6 ± 9.6	52.1 ± 9.2		
	ConA − 0.06	83.9 ± 6.2	84.3 ± 14.0		
	LPS − 5.0	25.0 ± 4.4	26.4 ± 4.8		
	PWM − 1:100[a]	19.7 ± 3.2	25.1 ± 4.1		
6	0	3.4 ± 0.5	1.9 ± 0.4[b]	0.5 ± 0.1	0.7 ± 0.2
	PHA − 0.125	59.3 ± 5.3	65.4 ± 2.8	54.5 ± 3.3	47.2 ± 4.6
	ConA − 0.06	56.7 ± 5.5	58.6 ± 5.1	75.7 ± 3.8	70.5 ± 4.2
	LPS − 5.0	17.4 ± 1.8	24.3 ± 4.5	13.4 ± 1.7	15.0 ± 1.4
	PWM − 1:100[a]	18.7 ± 2.1	29.1 ± 4.8	18.8 ± 1.3	19.6 ± 1.4

Numbers in parentheses are number of mice treated.
[a]Dilution of pokeweed mitogen.
[b]$P < 0.05$, Student's t-test.

Table 4 Natural killer cell activity of 3- and 6-week-old mice born to dams irradiated with 2450 MHz

Age (weeks)	$E:T$ Ratio[a]	Mean Percent ^{51}Cr Release ± SE Exp. No. 1 Sham(7)	Exp. No. 1 Irradiated(7)	Exp. No. 2 Sham(11)	Exp. No. 2 Irradiated(11)
3	25:1	6.3 ± 1.3	6.4 ± 2.1	8.5 ± 1.9	8.3 ± 1.6
	50:1	9.1 ± 2.0	9.4 ± 3.1	12.0 ± 2.4	7.8 ± 1.8
	100:1	9.4 ± 1.9	10.7 ± 3.8	15.4 ± 3.3	11.7 ± 3.1
6	25:1	16.2 ± 2.6	12.4 ± 2.8	7.4 ± 1.2	5.3 ± 0.5
	50:1	19.2 ± 4.0	13.5 ± 3.1	11.8 ± 1.8	8.2 ± 0.9[b]
	100:1	22.1 ± 3.8	16.6 ± 2.9	14.5 ± 1.9	9.8 ± 1.1

Numbers in parentheses are number of mice treated.
[a]Effector (spleen cells): target cell (YAC-1) ratio.
[b]$P < 0.05$, Student's t-test.

The results of the natural killer (NK) cell assay are shown in Table 4. While a significant ($P < 0.05$) reduction in NK activity was observed for only one of the $E:T$ cell ratios for 6-week-old mice, in the second experiment the data suggest a reduction in NK activity in mice irradiated with 2450 MHz *in utero*. In both experiments a reduction in NK activity was observed for all $E:T$ cell ratios for 6-week-old mice. There was a great amount of variability in NK activity among mice within a given group. This is due to the fact that CD-1 mice are non-inbred and may account for the lack of a robust difference in NK activity between sham and irradiated mice. A significant ($P < 0.05$) suppression in NK activity has been observed in adult mice irradiated for either 2 or 9 consecutive days at 30 mW/cm^2, but not at 5 or 15 mW/cm^2 2450 MHz, with similar suppression following injection of hydrocortisone (unpublished results). These results are similar to those reported by Cain et al. [1980] in which adult hamsters showed depressed NK activity at 25 mW/cm^2 but not at 15 mW/cm^2 2450 MHz microwaves. On the other hand, they are in contrast to a report by Schlagel et al. [1979], in which NK activity in neonatal mice irradiated with 2450 MHz was reported to be significantly ($P < 0.01$) enhanced compared with sham-irradiated mice.

NK cells have been implicated as being an important effector mechanism in tumor cell cytolysis *in vitro*. These cells display a spontaneous cytotoxic reactivity against syngeneic and allogeneic tumor cells in the absence of immunological priming and, as such, have been suggested to play a significant role as a first line of defense against newly arising malignant cells [Herberman et al., 1979]. Since these cells may play an important role in defense against certain neoplasms, further work is necessary to explain reported discrepancies in NK activity following microwave exposure.

The power density (28 mW/cm^2) employed in the present study is obviously thermogenic. The absorbed dose rate (16.5 W/kg) is more than twice the basal metabolic rate of a mouse (i.e., 6.4 W/kg [Kleiber, 1975]). The thermogenic potential of microwaves has been demonstrated in adult mice whose thermoregulation has been impaired by injection with 5-hydroxytryptamine (5-HT). At a power density as low as 1 mW/cm^2, irradiation of mice at 2450 MHz for 15 minutes caused a significant increase in core temperature compared with sham-irradiated 5-HT treated mice [Smialowicz et al., 1981c]. While no consistent change in immune function was observed in this study, the results suggest that NK cell activity may be affected. Further studies are required to corroborate the work of Berman et al. [1978, 1981] on microwave-induced stunting in mice and to determine if there is a causal relationship between neonatal stunting and an impairment in the development of NK cell activity.

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REFERENCES

Berman, E., J. B. Kinn and H. B. Carter (1978). Observations of mouse fetuses after irradiation with 2.45-GHz microwaves. Health Physics, 35: 791–801.

Berman, E. and H. B. Carter (1981). Evidence for stunting in mice offspring as a result of *in utero* exposure to 2450-MHz microwaves. Bioelectromagnetics (In press).

Cain, C. A., H-Y. Yang, G. Rama Rao, S. Fan, R. L. Magin and W. A. F. Tompkins (1980). Effect of *in vivo* microwave exposure on the hamster immmune system. Bioelectromagnetics, 1: 246.

Elder, J. A. and J. S. Ali (1975). The effect of microwaves (2450-MHz) on isolated rat liver mitochondria. Ann. N.Y. Acad. Sci. 247: 251–262.

Herberman, R. B., J. Y. Djeu, H. D. Kay, J. R. Ortaldo, C. Riccardi, G. D. Bonnard, H. T. Holder, R. Fagnoni, A. Santoni and P. Puccetti (1979). Natural killer cells: Characteristics and regulation of activity. Immunological Rev. 44: 43–70.

Helwig, J. T. and K. A. Council (1979). The SAR User's Guide. SAR Institute, Inc., Raleigh, N.C.

Jerne, N. E. and A. A. Nordin (1963). Plaque formation in agar by single antibody-producing cells. Science, 140: 405.

Kiessling, R., P. Hochman, O. Haller, G. M. Shearer, H. Wigzell and G. Cudkowicz (1977). Evidence for a similar or common mechanism for natural killer cell activity and resistance to hemopoietic grafts. Eur. J. Immunol. 7: 655–663.

Kleiber, M. (1975). The Fire of Life. An Introduction to Animal Energetics. pp. 179–236. Robert E. Kreiger Publishing Co., Huntington, NY.

Schlagel, C., T. Foths, J. Woody, W. Leach, and K. Sulek (1979). Enhancement of natural killer cell activity in mice after exposure to microwave radiation. Fed. Proc. Abstract No. 3625.

Smialowicz, R. J., J. B. Kinn and J. A. Elder (1979a). Perinatal exposure of rats to 2450-MHz CW microwave radiation: Effects on lymphocytes. Radio Science, 14(6S): 147–153.

Smialowicz, R. J., M. M. Riddle, P. L. Brugnolotti, J. M. Sperrazza and J. B. Kinn (1979b). Evaluation of lymphocyte function in mice exposed to 2450-MHz (CW) microwaves. *In* Proceedings of the 1978 Symposium on Electromagnetic Fields in Biological Systems (S. S. Stuchley, Ed.) Ottawa, Canada, pp. 122–152.

Smialowicz, R. J., J. S. Ali, E. Berman, S. J. Bursian, J. B. Kinn, C. G. Liddle, L. W. Reiter and C. M. Weil (1981a). Chronic exposure of rats to 100-MHz (CW) radiofrequency radiation: Assessment of biological effects. Radiat. Res. 86: 488–505.

Smialowicz, R. J., C. M. Weil, J. B. Kinn and J. A. Elder (1981b). Exposure of rats to 425-MHz (CW) microwave radiation: Effects on lymphocytes. J. Microwave Power (Submitted for publication).

Smialowicz, R. J., M. M. Riddle, P. L. Brugnolotti, R. R. Rogers, and K. L. Compton (1981c). Detection of microwave heating in 5-hydroxytryptamine-induced hypothermic mice. Radiat. Res. 88: 108–117.

Vos, J. G. (1977). Immune suppression as related to toxicology. CRC Crit. Rev. Toxicol. 5: 67–101.

Wilson, J. G. (1973). Environment and Birth Defects. Academic Press, Inc., New York, pp. 11–34.